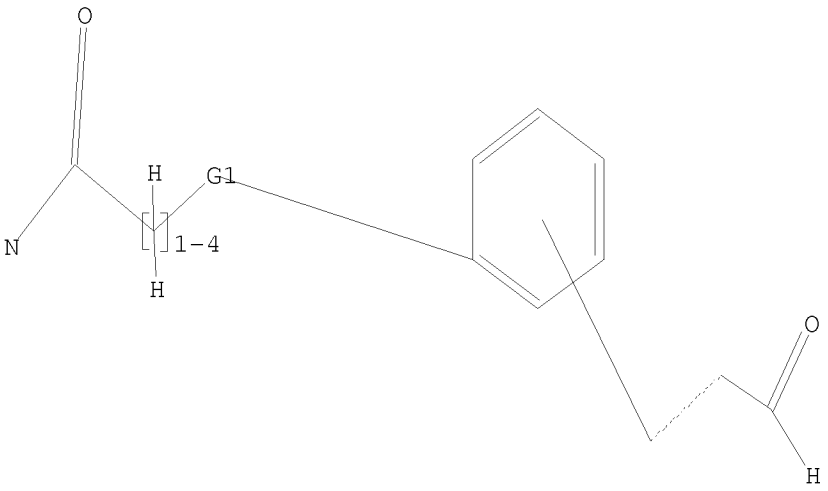
10/518,777

```
=>
Uploading C:\Program Files\Stnexp\Queries\10518777a.str

L1      STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1              STR
```

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G1 O,S


Structure attributes must be viewed using STN Express query preparation.


=> s l1 full
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.




FULL SEARCH INITIATED 18:57:41 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -  1805703 TO ITERATE

 55.4% PROCESSED  1000000 ITERATIONS                                2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.09

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:      1805703 TO  1805703
PROJECTED ANSWERS:               2 TO        8

L2            2 SEA SSS FUL L1



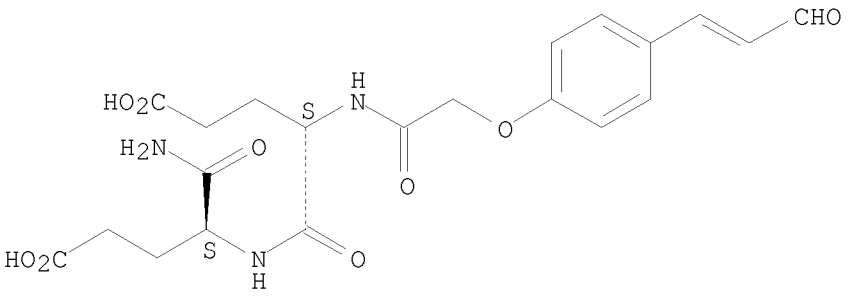
TOh                                  02/03/2008
```

L3 2 L2

=> d 1-2 ibib abs hitstr

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:51801 CAPLUS
DOCUMENT NUMBER: 140:299276
TITLE: Peptidyl aldehydes as slow-binding inhibitors of dual-specificity phosphatases
AUTHOR(S): Park, Junguk; Fu, Hua; Pei, Dehua
CORPORATE SOURCE: Department of Chemistry, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2004), 14(3), 685-687
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Peptidyl aldehydes were tested for inhibition of dual-specificity phosphatases VH1 and VHR. The most potent compound, cinnamaldehyde-Gly-Glu-Glu (Cinn-GEE), acted as a slow-binding inhibitor with KI* of 18 and 288 μM against VH1 and VHR, resp.
IT 676474-34-3
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(peptidyl aldehydes as slow-binding inhibitors of dual-specificity phosphatases)
RN 676474-34-3 CAPLUS
CN L-α-Glutamine, N-[[4-(3-oxo-1-propenyl)phenoxy]acetyl]-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

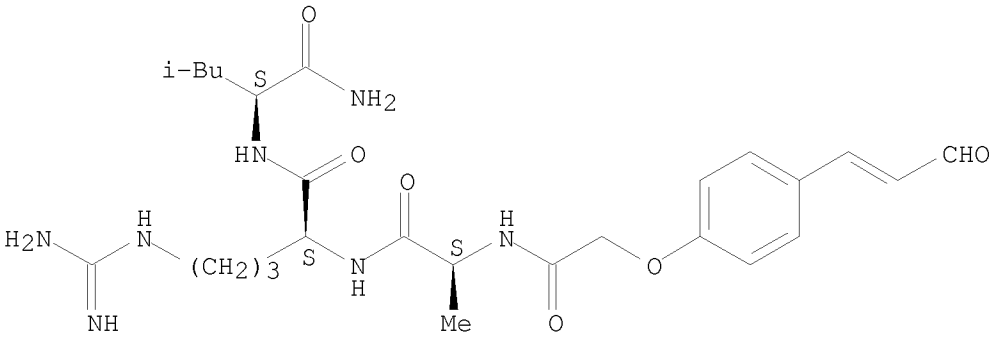


REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:282922 CAPLUS
DOCUMENT NUMBER: 139:18929
TITLE: Peptidyl Aldehydes as Reversible Covalent Inhibitors of Src Homology 2 Domains

AUTHOR(S): Park, Junguk; Fu, Hua; Pei, Dehua
CORPORATE SOURCE: Department of Chemistry and Ohio State Biochemistry Program, Ohio State University, Columbus, OH, 43210, USA
SOURCE: Biochemistry (2003), 42(17), 5159-5167
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:18929
AB Src homol. 2 (SH2) domains are phosphotyrosine- (pY-) binding modules found in a variety of signal-transducing proteins and constitute an important class of drug targets for the treatment of signaling related diseases/conditions. To date, a large number of peptidic as well as nonpeptidic SH2 domain inhibitors have been reported. However, all of these inhibitors contain a neg. charged pY mimetic as the core structure and generally have poor membrane permeability. We report here that peptidyl cinnamaldehydes function as reversible, slow-binding inhibitors toward the SH2 domains of protein tyrosine phosphatase SHP-1. Specific interactions between the SH2 domains and the aldehydes were assessed by their ability to relieve the autoinhibitory effect of the N-terminal SH2 domain on SHP-1 catalytic activity and the surface plasmon resonance technique. The most potent inhibitor (Cinn-GEE) displayed a KD value of 1.3 μM against the N-terminal SH2 domain of SHP-1. The mechanism of inhibition was investigated by site-directed mutagenesis and by using Cinn-GEE specifically labeled with 13C at the aldehyde carbon and 1H-13C heteronuclear single-quantum coherence spectroscopy. The proposed mechanism involves the formation of an initial noncovalent E·I complex, which is slowly converted into a covalent imine/enamine adduct (E·I*) between the aldehyde group of the inhibitor and the guanidine group of Arg βB5 in the pY-binding pocket of the SH2 domains. These aldehydes should provide a general, neutral pharmacophore for the further development of potent, specific, and membrane-permeable SH2 domain inhibitors.
IT 537036-71-8P
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(peptidyl aldehydes as reversible covalent inhibitors of src homol. 2 domain of protein tyrosine phosphatase SHP-1)
RN 537036-71-8 CAPLUS
CN L-Leucinamide, N-[[4-(3-oxo-1-propenyl)phenoxy]acetyl]-L-alanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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